REMARKS/ARGUMENTS

Reconsideration of this application, as amended, is respectfully requested.

Claims 31-33 were pending and have been rejected in the present application.

With the present amendments, claim 31 has been canceled. Claim 32 and 33, previously dependent on claim 31, have been amended to make them independent. No new matter is added to this application with these amendments, and their entry is respectfully requested.

The Examiner noted that Applicant's amendment, filed May 4, 2004, with respect to the rejection of claim 33 under 35 USC §112, second paragraph, for use of the allegedly indefinite recitation, i.e., "ACAT," has been found persuasive, and this rejection has been withdrawn.

On August 3, 2004, Applicants submitted a Supplemental Information Disclosure Statement. Applicants respectfully request that the Examiner return a copy of the submitted forms PTO/SB/08A and PTO/SB/08B, marked as being considered and initialed by the Examiner.

CLAIM REJECTIONS – 35 USC § 112, FIRST PARAGRAPH

Claim 31, as previously amended, is rejected under 35 USC § 112, first paragraph, for scope of enablement because the specification, while being enabling for the particular compound of the formula in claims 32-33 herein employed in a method for treating Alzheimer's disease, allegedly does not reasonably provide enablement for the employment of any acyl-coenzyme A: cholesterol acyltransferase (ACAT) inhibitor to be administered for the claimed methods of the particular treatments herein in a patient, for reasons of record stated in the Office Action dated November 4, 2003. According to the Examiner, the recitation, "an acyl-coenzyme A: cholesterol acyltransferase inhibitor" or "an ACAT inhibitor," in claim 31 is seen to be merely functional language. The Examiner alleges that, in view of the *In re Wands* factors, the case *University of California v. Eli Lilly and Co.* (CAFC, 1997) and *In re Fisher* (CCPA 1970), to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test all compounds encompassed in the instant claims and their combinations to be administered to a host employed in the claimed methods of the particular treatments herein, with no assurance of success.

With the present amendments, in order to expedite prosecution of the present application, claim 31 has been canceled, without prejudice to the filing of a divisional application to the canceled subject matter. Therefore, Applicants assert that this rejection of claim 31 under 35 USC § 112, first paragraph, has been rendered moot and respectfully request the withdrawal of this rejection.

Also, Applicants would point out that, after the present amendment, claims 32 and 33 remain in the application. As noted above, the Examiner has admitted in the present Office Action that the specification is "enabling for the particular compound of formula in claim 32-33 herein employed in a method for treating Alzheimer's disease."

CLAIM REJECTIONS – 35 USC §103

Claims 31-33, as amended now in Paper No. 8 filed on August 12, 2003, are rejected under 35 USC § 103(a) as being unpatentable over Lee et al. (U.S. 5,491,172, of record) in view of Scolnick (WO 95/06470, of record) for reasons of record stated in the Office Action dated November 4, 2003. The Examiner alleges that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the instant compounds in methods of treating the onset of Alzheimer's disease herein. Thus, the Examiner concludes that the claimed invention as a whole is prima facie obvious over the combined teachings of the prior art.

As noted above, in order to expedite prosecution of the present application, claim 31 has been canceled, leaving claims 32 and 33 in the present application. The compounds in claims 32 and 33 are the compounds disclosed in the Lee reference, which is incorporated by reference in the present application. As noted in Applicants' previous responses, Lee discloses the use of these compounds for treating hypercholesterolemia and atherosclerosis. As acknowledged by the Examiner, Lee "does not expressly disclose that the instant claimed compound may be useful in a method of treating Alzheimer's disease." There is no mention of Alzheimer's disease in the Lee reference.

Also, as noted in Applicants' previous responses, Scolnick discloses that HMG-CoA reductase inhibitors (lovastatin, simvastatin, pravastatin and fluvastatin) may be useful to lower Apolipoprotein E isoform 4 (Apo E4) to treat and prevent Alzheimer's disease. Scolnick does not disclose or discuss the use of ACAT inhibitors in the treatment of Alzheimer's disease (AD), and certainly does not disclose or discuss the use of the compounds of Lee for the treatment of AD.

Therefore, Applicants respectfully assert that it would not have been obvious to one skilled in the art, in view of Lee and Sconick, that the compounds of claims 32 and 33, as amended, would be useful in the treatment of Alzheimer's disease. There was no motivation in either Lee or Scolnick to substitute these compounds in the methods of Scolnick to arrive at the presently claimed invention. Even if there were motivation to combine these references, there would not have been a reasonable expectation of success that these compounds would be useful for the treatment of Alzheimer's Disease. It is the present application that is the first disclosure that these compounds do indeed have this utility.

In the present Office Action, the Examiner again asserts that that the specification provides no factual data in working examples, i.e., testing results or data demonstrating that any ACAT inhibitors to be administered to a host or in vitro or in vivo are capable of treating Alzheimer's disease. The Examiner suggests that Applicants provide clear and convincing evidence of nonobviousness or unexpected results to rebut the prima facie obviousness rejection.

As explained above and in Applicants' previous responses, the Examiner has not established a *prima facie* case of obviousness of the present application, as amended, in light of the prior art references; therefore, no evidence of nonobviousness or unexpected results is required. However, as pointed out in Applicants' previous responses, Applicants have provided, in the specification, as filed, data for representative compounds of the present invention in well-recognized human and animal models for Alzheimer's disease (see Examples 1-3 and accompanying tables and figures at pages 10-18).

Applicants have shown that these compounds lower Aβ in Chinese Hamster Ovary (CHO) cells, which have been engineered to over-express human β-amyloid precursor protein (see Example 2, page16 to page 17, line10, and accompanying figures). More specifically, Applicants have shown that the compound, avasimibe (CI-1011), of claims 32 and 33, as amended, caused a substantial dose-dependent reduction in Aβ compared to the other compounds tested (see page 17, lines 7-10, and accompanying Figures 6A, B, C and D). As Applicants have noted previously, β-amyloid (Aβ) is the principal proteinaceous component of amyloid associated with Alzheimer's disease (AD), and Aβ is viewed as a likely underlying cause of the degeneration and dementia that characterizes AD.

Thus, Applicants in the present invention have unexpectedly found that the compounds of claims 32 and 33, as amended, are useful for the treatment of AD. Therefore,

Applicants submit that claims 32-33, as amended, are patentable over the Lee and Scolnick references, either singly or in combination, and respectfully request that this rejection of the claims under 35 USC § 103 be withdrawn.

On the basis of the above amendments and remarks, reconsideration of this application, as amended, and its early allowance are respectfully requested.

Respectfully submitted,

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